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FROM: Michael R. Ward
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Comments:

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SERIAL NO.: 10/006,290
FILING DATE: October 22, 2001
INVENTOR(S): Jay WOHLGEMUTH et al.
TITLE: LEUKOCYTE EXPRESSION PROFILING

Papers attached herewith:
1. **Transmittal - 1 page**
2. **Petition From Restriction Requirement - 6 pages**

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	10/006,290
Filing Date	October 22, 2001
First Named Inventor	Jay WOHLGEMUTH, M.D.
Art Unit	1634
Examiner Name	B. L. Sisson
Total Number of Pages in This Submission: 7	Attorney Docket Number: 506612000100

ENCLOSURES (*Check all that apply*)

- [ ] Fee Transmittal Form
  - [ ] Fee Attached
- [ ] Amendment/Reply
  - [ ] After Final
  - [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Document(s)
- [ ] Reply to Missing Parts/ Incomplete Application
  - [ ] Reply to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [x] Petition (From Restriction Requirement) - 6 pages
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
- [ ] Terminal Disclaimer
- [ ] Request for Refund
- [ ] CD, Number of CD(s) ____
  - [ ] Landscape Table on CD
- [ ] After Allowance Communication to TC
- [ ] Appeal Communication to Board of Appeals and Interferences
- [ ] Appeal Communication to TC (Appeal Notice, Brief, Reply Brief)
- [ ] Proprietary Information
- [ ] Status Letter
- [x] Other Enclosure(s) (please identify below):
  1. Fax Cover Sheet

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm Name	MORRISON & FOERSTER LLP (Customer No. 20872)		
Signature	Michael R. Ward		
Printed name	Michael R. Ward		
Date	10/12/06	Reg. No.	38,651

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted by facsimile to the Patent and Trademark Office, facsimile no. (571) 273-8300, on the date shown below.

Dated: 10/12/06 Signature: _____ (Victoria A. Wilson)

Docket No.: 506612000100
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Jay WOHLGEMUTH et al.

Application No.: 10/006,290 Confirmation No.: 8497

Filed: October 22, 2001 Art Unit: 1634

For: LEUKOCYTE EXPRESSION PROFILING Examiner: B. L. Sisson

PETITION FROM RESTRICTION REQUIREMENT

MS Petition
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

Applicants hereby petition the Commissioner to review the requirement for restriction in the above referenced application, as mailed September 23, 2005, and made "Final" in the Office Action mailed February 13, 2006. Specifically, Applicants request reconsideration of the restriction as applied to the ten (10) nucleic acid sequences recited in the claims of Group V.

Since Applicants made an election with traverse of Group V and SEQ ID NO: 4758 and requested reconsideration of the restriction requirement on November 22, 2005, Applicants have satisfied the statutory requirements for filing the instant petition.

I. Background to Petition

A restriction into eight (8) groups of claims was mailed September 23, 2005. In the restriction, the Examiner also articulated a "Sequence Restriction Requirement Applicable to Groups I-VII," requiring that Applicants elect a single sequence. As support for the rejection, the Examiner cited MPEP § 803.04, presumably for its characterization of nucleotide sequences

encoding different proteins as structurally distinct chemical compounds and the categorization of such sequences as "independent and distinct inventions within the meaning of 35 U.S.C. § 121."

Applicants respectfully disagree with the restriction requirement.

II. There is no serious burden on the Examiner

The Examiner appears to believe that a restriction requirement is proper simply because there are independent or distinct inventions. However, this is simply not the law. A restriction requirement is only proper when the inventions are independent or distinct *and* there would be a *serious* burden on the Examiner if restriction was not required. MPEP § 803(I).

The sequences at issue are short 50-mer sequences set forth in Table 8. In view of the existing widely available resources for sequence searching, a search of 10 such nucleic acids cannot be considered to constitute a serious burden. In order to search for relevant prior art, the Examiner merely needs to copy the sequences in the present claims, paste them into an Internet database, and select the search button or hit the "enter" key.

Furthermore, under section 803.02 of the MPEP, if the members of a Markush group can be examined without serious burden, the Examiner must examine all members even though they may be directed to independent and distinct inventions. A limited number of Markush members or a close relation between Markush members can support a finding that a search can be made without serious burden. MPEP § 803.02. Present claim 55 is directed to a Markush group of 10 nucleic acid sequences. Although the MPEP fails to offer guidelines as to what size of Markush group is small enough to avoid incurring a serious burden on the PTO, surely it is safe to assume that 10 nucleic acid sequences, which has been deemed to be a generally reasonable number for examination purposes in MPEP §803.04, would also be small enough to satisfy the Markush group "undue burden" test for a restriction requirement.

Since the Examiner faces no serious burden when examining the ten nucleic acid sequences, Applicants respectfully submit that the restriction requirement is improper and request withdrawal of the requirement.

III. The burden on Applicants and society far exceeds the burden on the PTO

As made clear by § 803.04, the section of the MPEP setting forth special rules for restriction of nucleotide sequences, the burden on Applicants should also be considered when determining whether to issue a restriction requirement, particularly with respect to biotechnology companies.

The burdens of restricting the pending claims to a single sequence are particularly acute in this case. Applicants not only face the long development times faced by all biotechnology companies, but also work at a small start-up company with limited resources. The Examiner's maintenance of the restriction requirement will force Applicants to incur the expense of filing nine (9) additional divisional applications, each of which will cost approximately $10,000 to prepare, file and prosecute. The initial cost of filing the application will be further compounded by the additional maintenance and docketing costs for each application. All of these additional costs, which are a direct result of the restriction requirement, will place a severe financial burden on Applicants.

Given the limited resources of Applicants, such a financial burden will have substantial effects on the company, potentially forcing the company to downsize and limiting its ability to serve society by practicing its invention. Applicants' claimed invention is a method for monitoring or diagnosing transplant rejection by detecting the expression level of certain nucleic acids. A biopsy, the traditional method for detection of transplant rejection, is time-consuming, painful, and can involve the added risks of infection, organ damage and organ puncture. With the present invention, it is no longer necessary to subject transplant patients to multiple biopsies. Applicants' Allomap™ molecular expression test, an embodiment of this invention, is currently used to analyze samples from over 20 medical centers.

In addition to imposing significant financial costs, maintenance of the restriction requirement will also impair outside investment in the company, an essential source of working capital for small start-up companies like the one at which Applicants work. Parties will not invest in a company unless they believe they will obtain a fair return on their investment. A patent allows Applicants to reassure investors that they will have a period of exclusivity during which they will enjoy the unparalleled competitive advantage of being the only party on the market with a particular invention.

Finally, in addition to the burden on Applicants themselves, the Examiner's insistence on maintaining the restriction requirement also places a significant burden on society. As mentioned previously, the financial pressures on Applicants will limit availability of this invention to society. Furthermore, by restricting the present application so that a single sequence is the subject of each application, the Examiner is burdening the PTO with examination of ten applications instead of a single application. This duplication of effort wastes the time of the PTO's employees, who we understand are already burdened by the increasing number of applications being filed. **If the PTO cannot handle its existing workload, why force applicants to file nine divisional applications?**

As described above, if the restriction requirement is withdrawn, the Examiner simply needs to copy the text of each of the nine remaining sequences provided in the claims and perform an Internet search in order to examine the sequences of the claims. In light of the significantly larger burdens on Applicants and society imposed by the restriction requirement, Applicants respectfully request that the restriction requirement be withdrawn.

IV. Under the current MPEP guidelines relating to restriction of nucleotide sequences, ten sequences should be examined

In the case of nucleotide sequences, the PTO has officially recognized that "normally ten sequences" [can] ... constitute a reasonable number for examination purposes," and explicitly states that its rationale is to aid the biotechnology industry. MPEP § 803.04. The MPEP presents this as a general rule, conceding only that in some exceptional cases will the complex nature of the claimed material require that the reasonable number of sequences to be selected to be less than ten. MPEP §

803.04. As an example of what type of invention is considered to have a complex nature, the MPEP cites a claimed protein amino acid sequence reciting three dimensional folds.

The presently claimed invention is a method for diagnosing or monitoring transplant rejection in a patient comprising determining the expression level of a nucleic acid, where the nucleic acid comprises a nucleic acid selected from the group consisting of SEQ ID NO: 3702, SEQ ID NO: 2073, SEQ ID NO: 213, SEQ ID NO: 3028, SEQ ID NO: 4758, SEQ ID NO: 6299, SEQ ID NO: 832, SEQ ID NO: 2143, SEQ ID NO: 3651, and SEQ ID NO: 3750. The claimed sequences are nucleic acids without any particular structural limitations beyond the nucleotide sequence. By any measure, it is difficult to see how one could consider such sequences to have a complex nature that would require the number of sequences to be limited to less than ten.

Furthermore, the PTO has previously found claimed sequences having a nature similar to those in the present case to be sufficiently simple to be examined in a single application. Currently pending application 10/325,899 assigned to Expression Diagnostics, Inc., has pending claims directed to ten nucleic acid sequences undergoing active prosecution. The present Examiner has failed to offer any reason why the sequences of 10/325,899 are suitable for examination in a single application, while the presently claimed sequences are not.

Thus, given the special MPEP guidelines relating to examination of nucleotide sequence claims, the presently claimed ten nucleic acid sequences should be rejoined and subject to examination.

V. Conclusion

In view of the above, Applicants respectfully assert that all ten sequences in the Markush group cited in claim 55 should be examined together. Given the existing Internet databases for sequence searching, examination of all 10 sequences in a single application will not constitute a serious burden on the Examiner. Moreover, this burden is very slight compared to the burden placed on Applicants and society by filing nine additional applications. Finally, the PTO itself has recognized that ten sequences will normally constitute a reasonable number of sequences for

examination purposes and in particular, has recognized this for sequences having a structure similar to those under examination in this application. Accordingly, Applicants request withdrawal of the restriction requirement and joinder of all ten sequences listed in claim 55 as amended in the response filed May 15, 2006.

Applicants have timely traversed the restriction requirement in this application. Applicants have submitted this petition within the time limits imposed by 37 C.F.R § 1.144. We have not identified a fee associated with this petition. If this is incorrect, the Commissioner is authorized to charge the cost of such fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 506612000100.

Dated: 10/12/2006

Respectfully submitted,

By Michael R Ward

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